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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/027,205	02/20/1998	CARL H. JUNE	36119-126	2825

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WILMER CUTLER PICKERING HALE AND DORR LLP
60 STATE STREET
BOSTON, MA 02109

EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/027,205	JUNE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/5/04; 8/5/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *96,97 and 99-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *96,97 and 99-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 3/5/04, has been entered.
Claims 1-94 have been canceled.
Claims 95-107 have been added

Applicant's amendment, filed 8/5/04, has been entered.
Claims 95 and 98 have been canceled.
Claims 99-107 have been amended

Claims 96-97 and 99-107 are pending in the instant application.

2. The previous rejections under 35 USC 112, first paragraph, 102, 103 and obvious double patenting have been withdrawn in view of applicant's arguments and amended claims, filed 3/5/04 and 8/5/04, particularly with respect to the positive step of "measuring the level of CCR5 expression in said contacted T cell".

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 96-97 and 99-107 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "antigen binding fragments that bind either CD3 or CD28"; does not reasonably provide enablement for any "fragment thereof" of an anti-CD3 or anti-CD28 antibody.
The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has not provided sufficient direction and guidance as to any "fragment thereof" of an anti-CD3 or anti-CD28 antibody that would retain the specificity and function of anti-CD3 or anti-CD28 antibody and, in turn, bind CD3 or CD28 and downregulate CCR5 expression in a T cell, encompassed by the claimed methods.

While "fragment" may have some notion of the activity of the antibodies employed in the claimed methods; there is insufficient direction and guidance as to the structural nature or properties to enable any fragment of an anti-CD3 or anti-CD28 antibody to downregulate CCR5 expression in inhibit graft rejection. For example, such "fragment" could read on an Fc portion of an antibody that does not bind CD3 or CD28 and, in turn, would not be predictive to downregulate CCR5 expression in a T cell.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any "fragment" of anti-CD3 or anti-CD28 antibodies antibodies other than those that bind CD3 or CDCD28 and downregulate CCR5 expression in T cells.

Applicant is invited to amend the claims to recite "antigen-binding fragments" to obviate this rejection.

5. Claims 96-97 and 99-107 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "measuring CCR5 mRNA or protein", does not reasonably provide enablement for "measuring CCR5 expression by any other parameter".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification provides sufficient direction and guidance for measuring CCR5 mRNA and protein by a variety of assays (e.g. pages 27 – 29).

However, the specification does not provide sufficient direction and guidance as how to measure the level of CCR5 expression in contacted T cell by any other parameter.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any parameter by which to measure the level of CCR5 expression in contacted T cells other than by measuring CCR5 mRNA and protein.

Applicant is invited to amend the claims to recite "measuring CCR5 mRNA and protein" to obviate this rejection.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 96-97 and 99-107 are rejected under 35 U.S.C. § 103(a) as being unpatentable over June et al. (U.S. Patent No. 6,352,694) (of record) in view of Levine et al. (Science 272: 1939-1942, 1996) (of record), Chang et al. (U.S. Patent No. 6,129,916) (of record) and newly added Kwon et al. (U.S. Patent No. 5,569,997) and Allaway et al. (US 2004/0086528 A1).

The teachings of June et al. (U.S. Patent No. 6,352,694) in view of Levine et al. (Science 272: 1939-1942, 1996) and Chang et al. (U.S. Patent No. 6,129,916) are of record. A more thorough review of applicant's arguments and the examiner's rebuttal of record with respect to these teachings can be found in the previous Office Actions. June et al. in view of Levine et al. and Chang et al. differ from the claims not measuring the level of CCR5 expression in T cells contacted with anti-CD3 and anti-CD28 antibodies.

Kwon et al. teach that the ligation of T cells with anti-CD3 and anti-CD28 antibodies induce an HIV virus resistant state, which appears to be specific for macrophage-tropic HIV and appears to be the result of down-regulation of CCR5, the fusion cofactor (see entire document, particularly column 28, paragraph 1).

Allaway et al. teach various methods to measure CCR5, including in assays measuring the effects of inhibiting fusion of HIV-1 to $CD4^+$ T cells and infection of the cells (see entire document, including Summary of the Invention).

Given the teachings of the beneficial effects of contacting T cells with anti-CD3 and anti-CD28 antibodies to increase HIV resistance and that this beneficial effect was a result of down-regulation of CCR5 as taught by the prior art, one of ordinary skill in the art at the time the invention was made would have been motivated to monitor the expression of CCR5 expression to monitor the effect of combining anti-CD3 and anti-CD28 antibodies on T cell populations on HIV expression. In addition, the prior art provides for the co-immobilization of anti-CD3 and anti-CD28 on the same bead as a means of stimulating T cells. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
February 9, 2004